

**EXPRESS MAIL LABEL # EL822429133US**

Form PTO-1390 REV.10-94)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEYS DOCKET NUMBER <b>RN99079</b>
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/elected office (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (IF KNOWN, SEE 37CFR 1.9) <b>10/019145</b> NOT APPLICABLE	
INTERNATIONAL APPLICATION NO. <b>PCT/FR00/01865</b>	INTERNATIONAL FILING DATE <b>June 30, 2000</b>	PRIORITY DATE CLAIMED <b>July 1st, 1999</b>	
TITLE OF INVENTION <b>PROCESS FOR PREPARING ORGANOZINC DERIVATIVES ELECTROCHEMICALLY, COMBINED WITH CATALYSIS WITH COBALT SALTS</b>			
APPLICANT (S) FOR DO/EO/US: <b>JACQUES PERICHON, CORINNE GOSMINI AND YOLANDE ROLLIN</b>			
Applicant herewith submits the United States Designated/Elected Office (DO/EO/US) the following items and other information:			
1 <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U S C 371 2 <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U S C 371 3 <input checked="" type="checkbox"/> This express request to begin national examination procedures (35 U S C 371) (f) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U S C 371 (b) and PCT Articles 22 and 39(1) 4 <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date  5 <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U S C 371(c)(2)) a. <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau). b. <input checked="" type="checkbox"/> has been transmitted by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US) 6 <input checked="" type="checkbox"/> A translation of the International Application into English (35 U S C 371(c)(2)). 7 <input checked="" type="checkbox"/> A copy of the International Search Report (PCT/ISA/210) 8 <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U S C 371(c)(2)). a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International b. <input type="checkbox"/> have been transmitted by the International Bureau c. <input type="checkbox"/> have not been made, however the time limit for making such amendments has NOT expired. d. <input checked="" type="checkbox"/> have not been made and will not be made. 9 <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U S C 371(c)(3)). 10 <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U S C 371(c)(4)). <b>(signed)</b> 11 <input checked="" type="checkbox"/> A copy of the International Preliminary Examination Report (PCT/IPEA/409). 12 <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U S C 371(c)(5)). <b>Items 13 to 18 below concern document(s) or information included:</b> 13 <input checked="" type="checkbox"/> An information Disclosure Statement under 37 CFR 1.97 and 1.98 14 <input checked="" type="checkbox"/> An assignment document for recording A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included 15 <input checked="" type="checkbox"/> A <b>FIRST</b> preliminary amendment 16 <input type="checkbox"/> A <b>SECOND</b> or <b>SUBSEQUENT</b> preliminary amendment 17 <input type="checkbox"/> A substitute specification. 18 <input type="checkbox"/> A change of power of attorney and/or address letter 19 <input checked="" type="checkbox"/> Certificate of Mailing by Express Mail 20 <input checked="" type="checkbox"/> Other items or information			
Forms <b>PCT/IB/306, 308 and 332, PCT/ISA/ 220 &amp; 210 (English &amp; French Version), PCT/IPEA/ 409 and 416 (English &amp; French Version), PCT/FR00/01865 as published</b>			

US APPLICATION NO. <b>10/019145</b> <small>(IF DOWN, SEE 37 CFR 1.53)</small>	International Application No. <b>PCT/FR00/01865</b>	ATTORNEY DOCKET NUMBER <b>RN99079</b>				
		<b>CALCULATIONS PTO ONLY</b>				
21 The following fees are submitted: <b>BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):</b> <input type="checkbox"/> Neither international preliminary examination fee (37 CFR 1,482) nor International search fee (37 CFR 1.445(a)(2) paid to USPTO and International Search Report not prepared by the EPO or JPO..... <b>\$1,040.00</b>  <input checked="" type="checkbox"/> International preliminary examination fee not paid to USPTO but International Search Report prepared by the EPO or JPO..... <b>\$ 890.00</b>  <input type="checkbox"/> International preliminary examination fee (37 CFR 1,482) not paid to USPTO but international search (37 CFR 1,445 (a)(2)) fee paid to USPTO..... <b>\$ 740.00</b>  <input type="checkbox"/> International preliminary examination fee paid to USPTO (37 CFR 1,482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) ..... <b>\$ 710.00</b>  <input type="checkbox"/> International preliminary examination fee paid to USPTO (37 CFR 1,482) and all claims satisfied provisions of PCT Article 33(2)-(4) ..... <b>\$ 100.00</b> <b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b>		<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;"><b>\$ 890.00</b></td> <td style="width: 50%;"></td> </tr> <tr> <td><b>\$ 0.00</b></td> <td></td> </tr> </table>	<b>\$ 890.00</b>		<b>\$ 0.00</b>	
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Surcharge of <b>\$130.00</b> for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1,492(e)).						
<b>CLAIMS</b>	<b>NUMBER FILED</b>	<b>NUMBER EXTRA</b>				
Total Claims	13-20=	0				
Independent Claims	4-3=	0				
MULTIPLE DEPENDENT CLAIMS(S) (if applicable) N/A		X\$18.00				
		X\$80.00				
		\$ 0.00				
		\$ 80.00				
		\$ 0.00				
		\$ 970.00				
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28)		\$ 0.00				
		\$ 970.00				
Processing fee of <b>\$130.00</b> for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1,492 (f)).		\$ 0.00				
		\$ 970.00				
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). <b>\$40.00</b> per property + <input type="checkbox"/>		\$ 40.00				
		\$ 1,010.00				
		Amount to be refunded \$				
		charged \$				

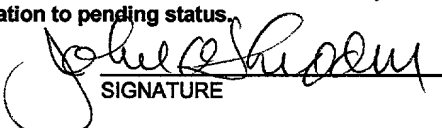
a ☐ A check in the amount of \$\_\_\_\_\_ to cover the above fees is enclosed

b ☒ Please charge my Deposit Account No. **18-1171** in the amount of **\$1,010.00** to cover the above fees.

c ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any  
 overpayment to Deposit Account No. **18-1171** A duplicate copy of this sheet is enclosed.

**NOTE: Where an appropriate time limit under 37 CFR 1,494 or 1,495 has not been met, a petition to revive (37 CFR 1.137 (a) or  
 (b)) must be filed and granted to restore the application to pending status.**

**SEND ALL CORRESPONDENCE TO:**  
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**John A. SHEDDEN**  
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**25,644**

**December 20, 2001**  
 DATE

REGISTRATION NUMBER

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**In the Application of: Jacques PERICHON, Corinne GOSMINI and Yolande ROLLIN**

**National Phase of PCT/FR00/01865**

**Examiner: N/A**

**International Filing Date : June 30 2000**

**Serial No: To be assigned**

**Art Unit: N/A**

**Filing Date: To be assigned**

**For: PROCESS FOR PREPARING ORGANOZINCIC DERIVATIVES  
ELECTROCHEMICALLY, COMBINED WITH CATALYSIS WITH  
COBALT SALTS.**

Commissioner for Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Dear Sir:

Prior to calculation of filing fee, please enter the following amendment in the specification and claims:

**In the Specification:**

Page 1, just after the title, please add the new following paragraph:

This application is an application under 35 U.S.C. Section 371 of International Application Number PCT/FR00/01865 filed on June 30, 2000.

**In the Claims:**

Please cancel claims 1-10, and replace them with the following new claims 11-23.

11. (New) A process of electrolytic synthesis of organozinc compounds, comprising the use of a catalytically amount of cobalt.

12. (New) The process according to claim 11, wherein, the organozinc compound is an aryl or vinyl organozinc compound.

13. (New) The process according to claim 11, wherein cobalt is present in an electrolyte in oxidation state II.
14. (New) The process according to claim 11, wherein cobalt is present in a coordinated form.
15. (New) The process according to claim 14, wherein cobalt is coordinated with a solutant or solvent compound that has a high donor number.
16. (New) The process according to claim 15, wherein the solutant or solvent compound comprises an atom having a high donor number, selected from the group consisting of atoms of the nitrogen column.
17. (New) The process according to claim 11, wherein cobalt is coordinated with a specific ligand.
18. (New) The process according to claim 17, wherein the ligand comprises a function selected from the group consisting of pyridine, nitrile, phosphine, stibine and imine functions.
19. (New) A composition for electrolytic use, comprising a cobalt salt, a zinc salt, a solvent and a cobalt ligand.
20. (New) A process for the electrolytic synthesis of an organozinc compound, comprising the step of subjecting to an electrolysis on an inert cathode a composition comprising a cobalt salt, a zinc salt, a solvent, a cobalt ligand, and an organic halide.
21. (New) A process according to claim 20, wherein the organozinc compound is an aromatic or vinyl organozinc compound.
22. (New) An aromatic organozinc compound comprising:

- an sp<sup>2</sup> carbon atom,
- at least one aniline group not more than monosubstituted,
- an SO<sub>2</sub> group, and
- a zinc-bearing function,

wherein the aniline group, the SO<sub>2</sub> group, and the zinc-bearing function are bounded to the sp<sup>2</sup> carbon atom.

23. (New) An aromatic organo zinc compound according to claim 22, wherein the sp<sup>2</sup> carbon atom is comprised in an aromatic group.

**REMARKS**


The preliminary amendments are filed to comply with the claims structure and wording according to the United States Patent law. It is asserted that these amendments do not add new matter. Support for these amendments can be found in the specification and claims as originally filed.

Entry of these amendments is respectfully requested.

Respectfully submitted,

December 20 , 2001

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F/RN99079 Prelim Amend.doc

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PCT/FR00/01865

**PROCESS FOR PREPARING ORGANOZINC DERIVATIVES  
ELECTROCHEMICALLY, COMBINED WITH CATALYSIS WITH COBALT  
SALTS**

The present invention relates to a novel  
5 process for synthesizing aryl organozinc derivatives.  
The invention relates more particularly to the  
electrolytic synthesis of aryl organozinc derivatives,  
in the catalytic presence of the element cobalt.

The reactivity of organozinc reagents,  
10 especially aryl organozinc reagents, shows many  
specificities which would make them particularly  
advantageous in many organic synthesis operations.  
However, they are difficult to obtain and are often  
prepared from organometallic reagents made with more  
15 electronegative metals, that is to say more reductive  
metals.

In addition, most of the techniques require  
the use of highly aprotic and especially very dry  
media.

20 In particular, reactions for the electrolytic  
synthesis of organozinc reagents present the risk of  
two unwanted reactions: firstly, the reduction reaction  
to give a hydrogenated derivative, and secondly, a  
coupling reaction (formation of biaryl).

25 A certain number of tests have been conducted  
in an attempt to perform this synthesis  
electrolytically. The tests that were the most

conclusive were performed by some of the authors of the present invention.

Mention may be made more particularly, firstly, of the general textbook "Organozinc reagent, a practical approach" (Paul KNOCHÉL and Philip JONES Editors, Oxford University Press, December 1998). More particularly, a synthetic route is described therein in chapter 8 by S. SIBILLE, V. RATOVELOMANANA and J. PERICHON (see also Journal of Chemical Society Chemical Communications, 1992, 283-284) and the article by C. GOSMINI, J.Y. NEDELEC and J. PERICHON (Tetrahedron Letters, 1997, 38, 1941-1942).

In these articles, the only route that is described therein is the use of very specific nickel complexes as electrolytic synthesis catalysts, in a limited number of media. However, the use of these nickel complexes, although constituting an important innovation, does not generally make it possible to achieve high yields relative to the haloaryl substrate.

Accordingly, one of the aims of the present invention is to provide a process for obtaining organozinc derivatives in good yields, both in terms of reaction yields (RY) and degrees of conversion (DC). In other words, one of the aims of the present invention is to provide a technique which allows the conversion of the substrate with good selectivity (CY).



Another aim of the present invention is to provide a technique for reducing the reduction and coupling reactions.

Another aim of the present invention is to  
5 provide a route that is capable of catalyzing the electrolytic synthesis reaction of aryl organozinc reagents, starting with the corresponding halo derivatives.

These aims and others, which will emerge  
10 hereinbelow, are achieved by means of using cobalt as a catalyst in the electrolytic synthesis of arylzinc compounds.

According to the present invention, it has been shown that cobalt can be introduced especially  
15 into the electrolyte in oxidation state II. Admittedly, cobalt can also be introduced in the form of cobalt III, but, since the medium is a reductive medium, this form will have a tendency to disappear very rapidly to be converted into various species, and  
20 especially into cobalt II. The state and form of the catalytically active cobalt have not been completely elucidated.

According to one preferred embodiment of the present invention, it is desirable to use cobalt in the  
25 presence of at least one of its ligands.

The coordination of the cobalt is advantageously performed with compounds (solvents or solvating agents) that have a high donor number. More

specifically, it may be pointed out that it is preferable that the donor number D of these solvents should be greater than or equal to 10, preferably less than or equal to 30, and advantageously between 20 and 5 30, the limits being included. The said donor number corresponds to the  $\Delta H$  (variation in enthalpy), expressed in kilocalories, of the combination of said aprotic polar solvent or of said ligand, with antimony pentachloride. This is described more specifically in 10 the book by Christian REINHARDT: "Solvents and Solvent Effects in Organic Chemistry - VCH, page 19, 1988". Said page gives a definition of the donor number.

It has been shown, in the course of the study which led to the present invention, that very good 15 results are obtained when the atom coordinating to the cobalt is an atom from the nitrogen column, and advantageously nitrogen. In this case, it is preferable that the ligand atom should not bear an electric charge.

20 When a specific coordinating agent is used, which does not act as solvent, pyridine, nitrile, phosphine, stibine and imine, or even oxime, functions or groups may be mentioned.

When unidentate (or monodentate) ligands are 25 used, it is desirable to use in the electrolyte a molar ratio between the ligand(s) and the cobalt which is high ( $[lig]/[Co]$  of about 10 and advantageously  $\geq$  about

100); there is usually no upper limit since the ligands may serve as solvent.

When bidentate or multidentate ligands are used, it is possible to decrease the lower limit to ratios at least equal to 2, advantageously to 4 and preferably to 6, but more preferably to 8.

To be efficient, it is desirable that the cobalt should be present at a minimum concentration at least equal to  $10^{-3}$  M. To be economical, it is preferable that the cobalt should not be too concentrated; thus, it is preferred that the cobalt content should be not more than 0.2 M.

The reaction medium advantageously comprises a solvent; this solvent should be polar enough to dissolve the metals or, more exactly, the metal salts used, and it should be lipophilic enough to at least partially dissolve the substrates from which it is desired to form the organozinc reagent.

It is preferable to use solvents that are sufficiently low in acidity (it is desirable that their pKa should be at least equal to 16, advantageously to 20 and preferably to 25), so that the reactions with hydrogen are as limited as possible. Thus, primary alcohols are too acidic to give very good results.

More specifically, the solvents that will be preferred are "polar aprotic" solvents such as, for example, alone or as a mixture:

- purely oxygenated solvents, in particular ethers, preferably polyethers such as 1,2-dimethoxyethane or cyclic ethers such as THF or dioxane;
- amides or ureas (DMF, N-methyl-2-pyrrolidone, imidazolidone, tetramethylurea, dimethoxypropyleneurea, etc.);
- sulfones (for example sulfolane) or sulfoxides (such as DMSO); and
- provided that they are liquid under the operating conditions, nitrogenous derivatives, nitrogenous heterocycles, especially pyridine, and compounds containing a nitrile function (for those that are preferred, see below); and
- provided that they are liquid under the operating conditions, complexing agents (crown ether, HMPT, tris(3,6-dioxaheptyl)amine (TDA-1)), which improve the correct functioning of the reaction by increasing the conductivity, increasing the reactivity of the anion and preventing the deposition of metal at the cathode.

Without this explanation being limiting, it would appear that these advantageous phenomena are correlated with the ability to complex the metal cations or as a mixture.

As has been mentioned previously, the solvents used may themselves act as complexing agents or ligands. They may especially, and advantageously,

contain one or more of the coordination functions mentioned above.

The solvent may be a mixture of an apolar solvent and a polar solvent as defined above by the  
5 donor number.

To make the products easier to separate from the reaction media, it is preferable that said solvent should have a boiling point that is substantially different from the compound to be synthesized and from  
10 the starting compound.

To facilitate the reaction and to improve the conductivity of the medium, saline electrolytes, occasionally referred to as base salts, optionally modified by the presence of complexing agents, are  
15 generally used. These electrolytes are chosen so as not to disrupt the reactions at the anode and the cathode.

According to one of the preferred embodiments of the present invention, an excess of zinc cation, relative to the stoichiometrically required amount, may  
20 be used as base salt, advantageously in the form of a fully dissociated salt (in general corresponding to an acid whose pKa is at most equal to 3, advantageously to 2, preferably to 1 and more preferably to zero).

When a soluble anode is used, the electrolyte  
25 may be chosen so as to have as cations those corresponding to the metals of the anode.

The electrolyte may be chosen so as to have as cations metals of high transporting power such as

divalent and advantageously trivalent metals, of the type such as aluminum, on condition that this does not disrupt the base reaction.

As metals used in the base salts, it is  
5 desirable to use those that have, besides the stage 0, only one stable oxidation state.

The electrolyte may be chosen such that these cations are directly soluble in the reaction medium. Thus, when the medium is sparingly polar, rather than  
10 making the metal cations soluble by means of adjuvants, it may be advantageous to use "oniums" that are stable in the electrical inactivity range.

The term "onium" means positively charged organic compounds, the name attributed to them by the  
15 nomenclature comprising an "onium" affix, generally a suffix (such as sulfonium [trisubstituted sulfur], phosphonium [tetrasubstituted phosphorus], ammonium [tetrasubstituted nitrogen]). The ones most frequently used are tetraalkylammoniums; the alkyl groups taken in  
20 their etymological sense generally contain from 1 to 12 carbon atoms and preferably from 1 to 4 carbon atoms. Phase-transfer agents may also be used.

The anions may be any common anions for inert electrolytes, but they are preferably chosen either  
25 from those released by the reaction, essentially halides, or, for example, from complex anions such as perfluoro bis-sulfonimides,  $\text{BF}_4^-$ ,  $\text{PF}_6^-$  or  $\text{ClO}_4^-$ . As a guide, it should be pointed out that DMF, used with, as

a base salt, tetrabutylammonium tetrafluoroborate at a concentration of 0.01 M, gives good results.

Another aim of the present invention is to provide a medium that may be used to perform the electrolysis and to give organozinc reagents. This aim has been achieved by means of a composition comprising at least:

- one cobalt salt,
- one zinc salt,
- 10 ▪ one conductive solvent, or a solvent that is made conductive, and
- one cobalt ligand.

The solvent and the cobalt ligand may be one and the same species, and even a single compound when the solvent is a single compound.

The cobalt content is advantageously between  $2 \times 10^{-1}$  and  $10^{-1}$  M and preferably between  $5 \times 10^{-3}$  and  $5 \times 10^{-2}$  M (closed interval, that is to say limits included).

Not taking into account the organozinc reagents formed, the zinc content is advantageously between 0.05 M and the solubility limit in the medium. When a soluble zinc anode is not used, it may be envisaged that a solid phase consisting of zinc salt(s) is present.

Said composition, when it is used to prepare organozinc reagents, also comprises an aryl halide whose preferred chemical characteristics will be given

later. This aryl halide is advantageously present in a concentration of from 0.1 to 1 M.

It is desirable that the molar ratio (dissolved species, needless to say not taking into account the organozinc reagents formed) of zinc to cobalt is between 100 and 1 and preferably between 10 and 2 (closed interval, that is to say limits included).

It is also recommended that the molar ratio (needless to say dissolved species, not taking into account the organozinc reagents formed) of zinc to aryl halide should be between 0.05 and 4 and preferably between 0.01 and 2 (closed interval, that is to say including the limits). The lowest values correspond to the case in which a soluble zinc anode is used.

According to one advantageous embodiment of the invention, the intensity and area of the reactive electrode, more exactly of the electrode at which the reaction takes place, are chosen such that the current density  $j$  is between 5 and  $5 \times 10^2$  A/m<sup>2</sup> and preferably between 20 and 200 A/m<sup>2</sup> (closed interval, that is to say including the limits).

By routine tests, a person skilled in the art can determine the reduction potential of cobalt in the reaction medium and that of the aryl halide. Once this determination is done, it will preferably be between the reduction potential of cobalt and that of the aryl halide.



The substrates which may be converted into organozinc reagents by the present invention represent a wide range of compounds. The halides are generally halides corresponding to relatively heavy halogens, 5 that is to say halogens heavier than fluorine.

It may also be mentioned as an indication that, when the halogen is linked to an electron-poor aromatic nucleus, it is preferable to use bromines or chlorines as halogen, chlorines being reserved for the 10 nuclei that are particularly electron-poor. If the condition is satisfied by six-membered heterocycles, in the case of homocyclic aryls, to use a chloride, it is preferable that the sum of the Hammett constants  $\sigma_p$  of the substituents (not taking the leaving halide into 15 account) should be at least equal to 0.40 and preferably to 0.50. On the other hand, the nuclei that are particularly electron-rich may use iodine as halide.

For further details regarding the Hammett 20 constants, reference may be made to the 3rd edition of the textbook written by Prof. Jerry March "Advanced Organic Chemistry" (pages 242 to 250) and published by John Wiley & Sons.

The five-membered heterocycles comprising a 25 chalcogen as hetero atom (such as furan and thiophene) have a large capacity to be converted into zinc reagents, show separate reactivity, and are always readily converted into zinc reagents. As a result, the

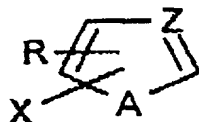
use of cobalt is less critical. In their case, the element cobalt makes it possible to obtain a monozinc reagent from dihalo compounds of the same rank.

The electron-poverty of the nucleus may be  
5 due either to the presence of electron-withdrawing groups as substituents, or, in the case of six-membered nuclei, to the replacement of a carbon with a hetero atom. In other words, the electron-poor nucleus may be a six-membered heterocyclic nucleus, especially  
10 heterocyclic nuclei containing an atom from the nitrogen column and more particularly nitrogen.

Among the electron-withdrawing groups that give good results, mention should be made of acyl groups, nitrile groups, sulfone groups, carboxylate  
15 groups, trifluoromethyl groups or, more generally, perfluoroalkyl groups and halogens lower in rank than the halide which will be converted into an organozinc reagent. When the substituents are halogens of the same rank, a diorganozinc reagent is generally formed. These  
20 diorganozinc reagents constitute novel compounds and correspond to the general formulae below in which X and R both represent zinc-bearing groups.

Among the donor groups, that is to say groups giving mediocre results with chlorine but good results  
25 with bromine, mention may be made of alkyloxy groups, alkyl groups, amine groups and dialkylamine groups.

The aromatic derivative which is the substrate in the present process advantageously corresponds to the following formula:



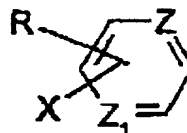
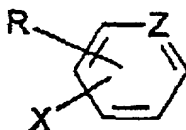
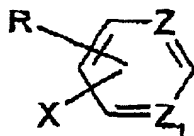
5 in which:

- Z represents a trivalent chain unit  $-C(R_1)=$ , an atom from column V, advantageously a nitrogen;
  - X represents the leaving halogen;
  - A represents either a chain unit chosen either
- 10 from the groups ZH or from chalcogens advantageously at least equal in rank to that of sulfur, or from the two-membered divalent unsaturated groups  $CR_2=CR_3$ ,  $N=CR_2$ ,  $CR_2=N$ .

Insofar as they are borne by contiguous

15 atoms, two of the radicals R,  $R_1$ ,  $R_2$  and  $R_3$  may be linked to form rings.

Thus, the aryls may especially be of formula:



in which Z1 is chosen from the same meanings as those

20 given for Z.

The radicals  $R_1$ ,  $R_2$  and  $R_3$  are chosen from the substituents mentioned above and especially:

- electron-withdrawing groups, in particular acyl groups, nitrile groups, sulfone groups, carboxylate

groups, trifluoromethyl groups or, more generally, perfluoroalkyl groups and halogens of a lower rank than the halide which will be converted into an organozinc reagent;

- 5    ■ donor groups, especially aryloxy or alkyloxy groups, hydrocarbyl groups such as aryls and alkyls (the latter word being taken in its etymological meaning) and amine groups, including groups monosubstituted and disubstituted with hydrocarbon-based alkylamine groups.
- 10

It is desirable that the substrates should contain not more than 50 carbon atoms, advantageously not more than 30 carbon atoms and preferably not more than 20 carbon atoms.

- 15    Among the substrates that are particularly advantageous are halides, preferably arylchlorides, bearing, especially in the metaposition, an aliphatic carbon (that is to say an  $sp^3$  carbon) bearing at least two fluorines. For example, the halides are preferably
- 20 trifluoromethylaryl chlorides.

This process for synthesizing organozinc reagents may be extended, firstly to all organozinc reagents linked to  $sp^2$ -hybridized carbon atoms and especially to the synthesis of organozinc reagents from

25 vinyl halides, especially when these vinyl halides are conjugated with aromatic nuclei.

Although the technique is economically much less advantageous, it may also be advantageous to note that it can also be transposed to aliphatic halides.

One of the advantages of the present invention is that it requires only complexing agents or ligands that are readily available, such as nitriles (preferably aromatic or bidentate) or pyridines and derivatives of the pyridine nucleus, such as quinoline. Moreover, bipyridyls, being bidentate, also give good results as ligands that are different from the solvent.

Although the bis-nitriles are capable of acting as bidentate ligands, they are poor complexing agents and should be used in high proportions of the same order as the monodentate ligands. They give good results.

It is desirable, in order to avoid the medium being too acidic, that the bis-nitriles constituting the solvent, some of the solvent, or the ligand, should be such that, via the most direct pathway, two nitrile functions are separated by at least two carbons and advantageously three carbons.

Dinitroalkylenes in which the alkylene group contains from 2 to 8 carbon atoms give good results. Mention may be made especially of glutaronitrile, methylglutaronitrile, adiponitrile, pimelonitrile and suberonitrile.

Another advantage of the present invention is its ability to be performed readily at room temperature and, more generally, at a temperature below 50°C.

Finally, the reaction does not require an  
5 inert electrolyte, since the zinc salt can be used as inert electrolyte.

Soluble zinc anodes may be used in this technique.

The present invention produces families of  
10 organozinc compounds corresponding to the preceding substrate formulae in which X has been replaced with a zinc-bearing function (generally noted -Zn- X' in which X' is halogen) which it has not been possible to obtain previously. Among the families of interest which it has  
15 not been possible to synthesize previously, mention should be made of the compounds derived from the preceding substrate formulae in which one of the radicals R, R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is a monosubstituted and especially an unsubstituted aniline function.

20 Mention may also be made of compounds in which one of the radicals R, R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> is a group bearing a sulfone group (-SO<sub>2</sub>-), including sulfonates, that is vicinal to the aromatic nucleus, that is to say that it is adjacent to it.

25 Finally, the dizinc compounds in which R is a zinc-bearing group.

The characteristics of these families may be cumulated to form preferred subfamilies.

The non-limiting examples which follow illustrate the invention.

General procedure (condition A)

Apparatus

- 5 Single-compartment electrolysis cell equipped with a zinc anode and a nickel sponge cathode (gold or stainless steel cathodes may also especially be used).  
Solvent: dimethylformamide/pyridine (45 ml/5 ml)  
Ambient temperature (20 to 25°)
- 10 Aryl halide: 10 millimoles  
Cobalt chloride: 1 millimole  
Zinc bromide: 2.5 millimoles  
Constant current: 0.2 A  
No inert electrolyte
- 15 Electrode area: 20 cm<sup>2</sup>  
Electrolysis time: 2 hours

The conditions differing from the general procedure are specified in the tables below, which give a sample of the results obtained.

- 20 The asterisk \* indicates that the yield measurement was performed by coupling the organozinc reagent with phenyliodide.

Example 1Table 1

In the case of aromatic halides



5

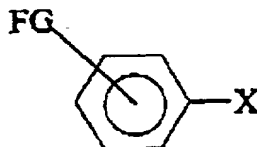
with FG = electron-donating group

FGArX	FGArZnX %	ArH %	ArAr	Comments
PhCl	6	?	0	84% PhCl remaining
PhBr	70	?	0	
PhI	20	Majority	0	
	82	18	0	All the PhI consumed
	75	21	0	
	62	37	0	
	6	20		74% ArCl remaining
	75	25	0	FG-Ar-Ph 70% Isolated*
	90	0	0	FG-Ar-Ph 85% Isolated*
	85		0	



Example 2Table 2

In the case of aromatic halides



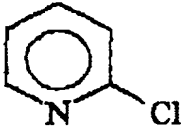
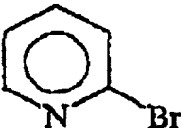
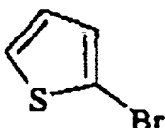
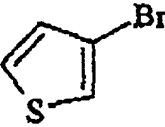
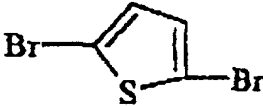
5

with FG = electron-withdrawing group

FGArX	ArZnX %	ArH	ArAr	Comments
	90	$\epsilon$	0	FG-Ar-Ph 80% Isolated
	85			
	58			19% ArBr remaining
	70			
	70 only 			
	60 monozinc derivative (ClPhZnBr)			
	79			disappearance of ArBr
	25			

Example 3Table 3

In the case of heteroaromatic halides

ArX	ArZnX %
	50
	25
	67
	25
	20 (monozinc derivative)

5

In general, the thiophene derivatives show exceptional reactivity and it was possible in this case to perform a monoconversion of a dibromo derivative.

Example 4

10

Table 4

In the case of aliphatic halides

RX	RZnX %	RH %	RY
$\text{CH}_3(\text{CH}_2)_3\text{Br}$	30	40	
$\text{Br}(\text{CH}_2)_3\text{COOEt}$	42		

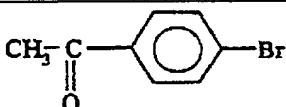
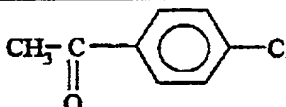
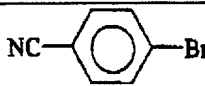
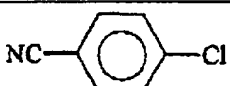
Example 5Table 5

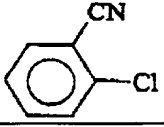
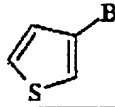
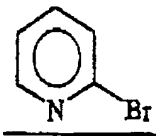
In the case of vinyl halide

Ph-CH=CHBr	PhCH=CHZnBr 45%
------------	-----------------

- The tests below were carried out by varying
- 5 the operating conditions such as the nature of the anode, the concentration of catalyst, the concentration of zinc salts, or by using 2,2'-pyridine as ligand instead of pyridine.

10 Example 6Table 6

ArX	ArZnX	Conditions
	75	CoCl <sub>2</sub> , 1 eq, ZnBr <sub>2</sub> , 2 eq, other conditions identical to A.
	50	CoCl <sub>2</sub> 0.2 eq, other conditions identical to A.
	75	CoCl <sub>2</sub> , 0.4 eq, other conditions identical to A.
	50	2 Bpy per Co, absence of pyridine, other conditions identical to A.
	77	ZnBr <sub>2</sub> , 2 eq, CoCl <sub>2</sub> , 1 eq, other conditions identical to A
	48	1 eq ZnBr <sub>2</sub> , iron anode, other conditions identical to A.
	70	ZnBr <sub>2</sub> , 2 eq, 1 eq CoCl <sub>2</sub> , other conditions identical to A.
	70	ZnBr <sub>2</sub> , 2 eq, 0.4 eq CoCl <sub>2</sub> , other conditions identical to A.
	50	ZnBr <sub>2</sub> , 2 eq, 0.4 eq CoCl <sub>2</sub> , other conditions identical to A.
	65	ZnBr <sub>2</sub> , 2 eq, CoCl <sub>2</sub> , 1 eq, other conditions identical to A.

	60	ZnBr <sub>2</sub> , 2 eq, CoCl <sub>2</sub> , 0.4 eq, other conditions identical to A.
	58	ZnBr <sub>2</sub> , 2 eq, CoCl <sub>2</sub> , 1 eq, other conditions identical to A.
	25	2 Bpy per CoCl <sub>2</sub> , absence of pyridine, other conditions identical to A

Example 7Formation of organozinc reagents from ethyl para-bromobenzoate, study of various solvents

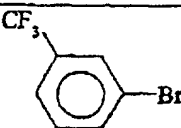
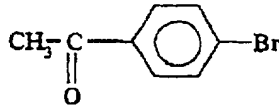
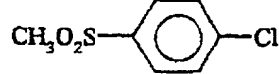
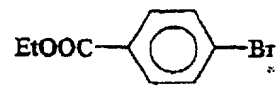
- 5 THF made conductive with tetrabutylammonium fluoroborate gives good results for organozinc reagents, although slightly lower than in dimethylformamide. The other amides such as dimethylacetamide also give good yields of organozinc
- 10 reagents. Nitriles such as acetonitrile give as much zinc reagent as when dimethylformamide is used.

Example 8

- The results obtained below were achieved in
- 15 an acetonitrile/pyridine mixture (45/5). The other conditions were identical to the general conditions.

Table 7

Electrosynthesis of organozinc reagents in  
acetonitrile/pyridine medium (V/V = 9/1)

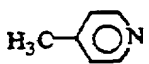
ArX	ArZnX
	80%
	57%
	90%
	80%

The use of benzonitrile instead of pyridine (9/1 mixture by volume) also leads to good results under the general conditions. In particular, starting with meta-bromofluorobenzene, a yield of 60% is obtained.

#### Example 9

##### 1. Ligands other than pyridine and benzonitrile


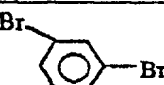
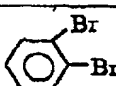
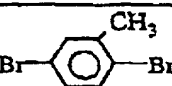
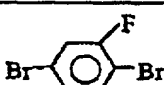
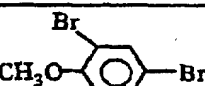
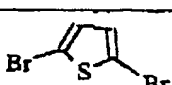
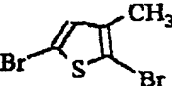
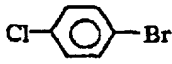

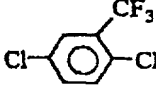
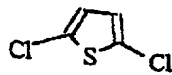
Starting with pBr-PhCO<sub>2</sub>Et under the general conditions described above (conditions A), the following results are obtained:

Solvent	Ligand	BrZnPhCO <sub>2</sub> Et
Acetonitrile (45 ml)	Adiponitrile (5 ml)	75 %
Acetonitrile (45 ml)	1,2 - dimethoxyethane (5 ml)	65 %
acetonitrile (45 ml)	 (5 ml)	50 %

2. Formation of aromatic and heteroaromatic dizinc reagents from aromatic dihalides (X-Ar-X)

General conditions identical to conditions A, but:

- the solvent is acetonitrile (45 ml)/pyridine (5 ml),
- $\text{CoCl}_2$  2 millimoles,
- electrolysis stopped after 4 Faradays have been passed per mole of X-Ar-X (4 hours)

X-Ar-X	X-ArZn (%)	XZn-Ar-ZnX (%)
	0	70
	0	51
	0	16
	0	66
	0	65
	0	44
	0	28
	0	28
	38 Pcl-Ph-ZnBr	30
	28	10
	73	19
	26	2

CLAIMS

1. The use of cobalt as a catalyst in the electrolytic synthesis of organozinc compounds, advantageously aryl or vinyl organozinc compounds.

5           2. The use as claimed in claim 1, characterized in that the cobalt is present in the electrolyte in oxidation state II.

          3. The use as claimed in claims 1 and 2, characterized in that the cobalt is present in a  
10 coordinated form.

          4. The use as claimed in claim 3, characterized in that the coordination of the cobalt is performed with a solutant or solvent compound that has a high donor number.

15           5. The use as claimed in claim 4, characterized in that the atom responsible for the good donor number is chosen from atoms of the nitrogen column.

          6. The use as claimed in claims 3 to 5,  
20 characterized in that the coordination of the cobalt is performed with a specific ligand.

          7. The use as claimed in claims 3 to 6, characterized in that said ligand contains functions chosen from pyridine, nitrile, phosphine, stibine and  
25 imine functions.



8. A composition for electrolytic use, characterized in that it comprises a cobalt salt, a zinc salt, a solvent and a cobalt ligand.

9. A process for the electrolytic synthesis of organozinc reagents, advantageously aromatic or vinyl organozinc reagents, characterized in that it consists in subjecting a composition as claimed in claim 8, also comprising an organic halide, to an electrolysis on an inert cathode.

10. An aromatic organozinc compound comprising directly linked to an  $sp^2$  carbon atom, that is advantageously aromatic, at least one function or group chosen from not more than monosubstituted aniline functions, an  $SO_2$  group and another zinc-bearing function.

**COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY**  
(include Reference to PCT International Applications) **PCT/ FR00/01865**ATTORNEY'S DOCKET NO  
**RN99079**

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**PROCESS FOR PREPARING ORGANOZINC DERIVATIVES ELECTROCHEMICALLY,  
COMBINED WITH CATALYSIS WITH COBALT SALTS**

the specification of which (check only one item below):

☐ is attached hereto.☐ was filed as United States application

Serial No. \_\_\_\_\_

on \_\_\_\_\_

and was amended

on \_\_\_\_\_ (if applicable)

☒ was filed as PCT international applicationNumber **PCT/ FR00/01865**on **June 30, 2000**

and amended under PCT ARTICLE 19

on \_\_\_\_\_ (if applicable).

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FRANCE	99/08480	July 1, 1999	<input checked="" type="checkbox"/> YES	<input type="checkbox"/> NO
			<input type="checkbox"/> YES	<input type="checkbox"/> NO
			<input type="checkbox"/> YES	<input type="checkbox"/> NO
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			<input type="checkbox"/> YES	<input type="checkbox"/> NO

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<b>Send Correspondence to:</b> <b>Kevin McVEIGH</b> <b>INTELLECTUAL PROPERTY DEPT.</b> <b>RHODIA INC.</b> <b>259 PROSPECT PLAINS ROAD,</b> <b>CN 7500,</b> <b>CRANBURY, NJ 08512-7500</b>			<b>Direct Telephone Calls to:</b> <small>(name and telephone number)</small> <b>Kevin McVEIGH</b> <b>(609) 860-4194</b>		
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